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"An Overview About Solid Lipid Nanoparticle For The Purpose Of Ocular Drug Delivery"

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ABSTRACT:

To get rid of certain drawbacks of traditional formulations, considerable attention has been paid to lipid-based drug delivery systems in recent years. Solid lipid nanoparticles (SLNs) and nano-structured lipid carriers (NLCs) are promising delivery systems among these because of their ease of manufacturing processes, ability to scale up, biocompatibility, and biodegradability of formulation constituents, as well as a number of additional benefits that may be related to a particular route of administration or the nature of the materials that are to be loaded onto these delivery systems. The use of many Nano-structured technologies for ocular medication delivery has shown some encouraging outcomes. During the 1990s, solid lipid nanoparticles (SLNs) have been investigated as possible drug delivery systems. Due to the fact that SLNs are made from physiological lipids, they do not exhibit bio toxicity. Since they may increase drug absorption via the cornea and increase the bioavailability of both hydrophilic and lipophilic medicines in the eye, SLNs are particularly helpful in the delivery of drugs to the eye. Another advantages of SLNs is that they allow autoclave sterilization, which is required before creating ocular preparations. This review outlines anatomy and physiology of eye, challenges in ocular drug deliver, brief overview about SLN with their application in common ocular diseases, future perspective of ocular drug delivery.

Keywords: *Solid Lipid Nanoparticle, Ocular Drug Delivery, Nano-particle, Nano structural Lipid Carrier*

1. INTRODUCTION

Due to the unique anatomy and physiology of the eye, drug delivery scientists and pharmacologists have faced significant difficulties. Static barriers (different layers of retina, sclera, and cornea including blood aqueous and blood–retinal barriers), dynamic barriers (choroidal and conjunctival blood flow, tear dilution, and lymphatic clearance), and efflux pumps in conjunction pose a significant challenge for delivery of a drug alone or in a dosage form, especially to the posterior segment. The study of influx transporters on various ocular tissues and the development of parent drug delivery strategies that target specific transporters have gained popularity in recent years.[1] The field of nanotechnology is one that has great potential for enhancing the effectiveness, compliance, and safety of ophthalmic medications. Once they are biodegradable and biocompatible, lipid based nanocarriers are one of the most interesting colloidal drug delivery technologies. They are now recognized as nanoscale carriers as a result.[2] Solid lipid nanoparticles (SLNs) and nano-structured lipid carriers (NLCs) are interesting carriers for ophthalmic applications.[3] The most serious ocular conditions, such as glaucoma, diseases that impact the posterior eye structures, or joint ocular disease inflammation or infection, can be treated with SLNs and NLCs. These technologies provide a novel concept that has been deemed a potential approach for treating various retinal illnesses.[4]They are fascinating because they enhance corneal permeability and boost bioavailability in ocular medication administration. In addition to these advantages, lipid nanoparticles (LNs) are also riskfree, noninvasive, and increase therapeutic benefits due to the longer residence period at the administration site, with little to no local side effects.[5]

Other attractive characteristics are the therapy safety, compliance, efficiency of ocular drugs, and versatility and compatibility. The adhesive qualities of lipid nanoparticles are also crucial for use in ocular medication administration, primarily because of their small size. Surface characteristics, especially mucosal surfaces, have a significant impact on the adhesive capabilities. These nanoparticles' surfaces are modified as a technique to increase the amount of time they are in contact with the cornea. Phospholipids, chitosan, cysteine-polyethylene glycol stearate conjugate, and stearylamine can all be used to create these surface changes. To improve muco-adhesion with anionic ocular tissues by electrostatic adhesion, cationic lipids, polysaccharide emulsifiers, or other moieties with cationic groups have been added to the lipid nano-particle composition.[6]

1.1 Anatomy And Physiology

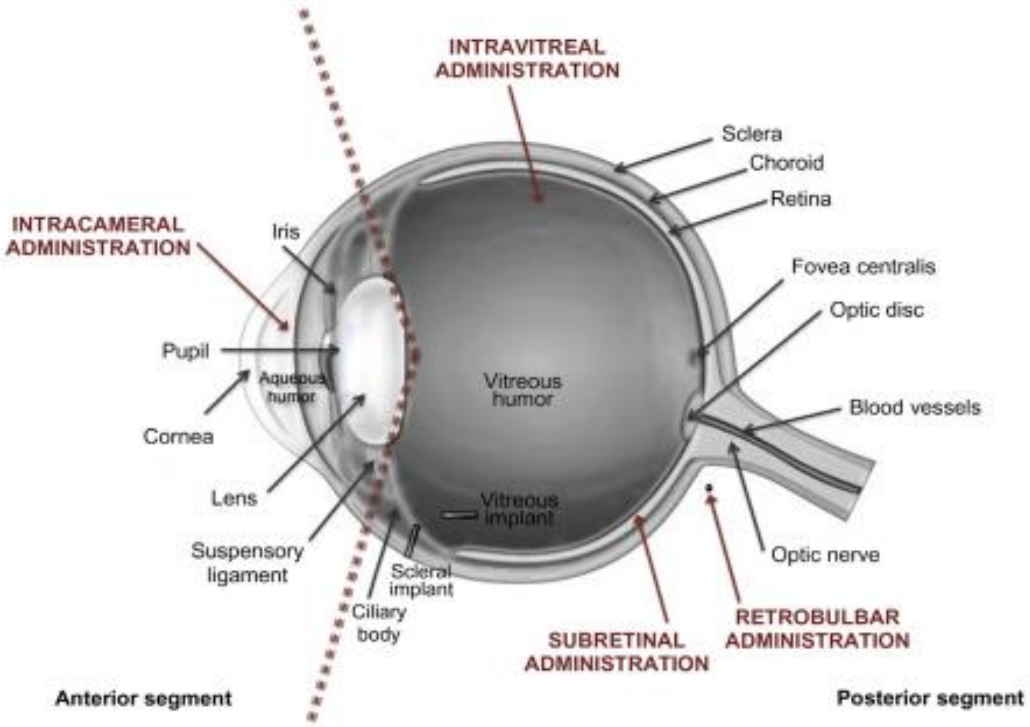

Fig No.1: Anatomy of Eye[7]

The human eye possesses a well-defined anatomy, divided into two regions (Fig.1): the anterior segment (conjunctiva, cornea, ciliary body, iris, the anterior and posterior chambers the lachrymal apparatus, the lens and the eyelids) and the posterior segment (choroid, sclera retina, and vitreous).[8,9] The outermost transparent and clear layer of the eye is called the cornea. It is made up of three layers—the stroma, endothelium, and epithelium—that are divided by Descemet's membrane and Bowman's layer but lack blood vessels. The conjunctiva, a thin, translucent, vascularized mucous membrane with a transparent surface, is where the cornea and sclera join into the covered region. It is here that the daisies are found, which are in charge of delivering secretory mucus containing solid lipid nano-particles to the eye. The anterior cornea's tear film, which covers the surface of the eye, is made up of mucus on the inside. [10] the outer layer of the tear film consists of a mixture of lipids secreted by the Meibomian glands eyelid.[11] the aqueous intermediate layer consists of a salt solution several proteins secreted mainly by lacrimal glands.[12,13]

Intraocular pressure is caused by the aqueous humor (IOP). [14] fills the anterior and posterior ventricles of the anterior segment. The anterior chamber is limited from the front by the cornea and a small part of the sclera; and behind the iris, lens, and part of the ciliary body. Iris and the lens borders the posterior chamber. At the back of the eye, the sclera is an opaque, slightly elastic fibrous protective layer. The composition of this layer is similar to that of the cornea, and it differs in the structural arrangement of collagen fibers. Scleral collagen has wider fibrils and a much more complex structure than the cornea. The sclera maintains intraocular pressure and acts as

an attachment point for the extraocular muscles that maintain the shape of the eye during eye movement.[15,16] The vitreal camera is surrounded by the retina and the lens (fig. 1). Diagram of the eye and the primary channels for ocular delivery.The location of the vitreous fluid in anatomy and physiology of the eye. Transparent and gelatinous, the vitreous humor preserves the structure of the eye while allowing light to reach the retina.[17] Several routes of administration are available for the target segment. Topical administration is an inexpensive way to treat diseases affecting the anterior part of the eye. In fact, conventional methods of ocular administration include solutions, suspensions, and creams, which account for nearly 90% of the ophthalmic formulations on the market. They have significant advantages such as ease of preparation, drug delivery and low production costs. They are also the vitreal camera is surrounded by the retina and the lens (fig. 1). Diagram of the eye and the primary channels for ocular delivery.The location of the vitreous fluid in anatomy and physiology of the eye. Transparent and gelatinous, the vitreous humor preserves the structure of the eye while allowing light to reach the retina. easy to use, resulting in high patient compliance and cost-effectiveness[18-20] When the goal is to deliver active compounds other tissues, such as the retina, require different routes of administration, such as systemic, intraocular, intraocular or intravitreal administration[21] However, when topical administration is considered, drugs formulated in the conventional ocular form have therapeutic efficacy. the number of drops is minimal due to anatomical barriers and physiological conditions that protect the eye from the penetration of foreign bodies.[22] First, a significant

portion of a topical drug is washed away by tears or eliminated by other mechanisms. To achieve a therapeutic effect in the treatment of diseases of the back of the eye, repeated administration of the ophthalmic preparation is necessary. This leads to a limited residence time of the drug on the cornea, which reduces the absorption of the drug and increases the cytotoxicity.[23,24] Some other limitations of eye drops include low drug bioavailability, inability to target specific ocular structures, and drug binding or inactivation of tear proteins. In addition, most active compounds have unfavorable physicochemical properties that prevent absorption and distribution in the eye tissues, drastically reducing the amount of drug reaching the target tissue.[22]

Table No. 1: Administration routes for posterior eye delivery.[25]

Route of Administration	Main Routes	Advantages	Disadvantages
Topical	Corneal and conjunctival-scleral pathway	Non-invasive drug delivery and high patient compliance. Minimal systemic side effects	Low availability due to clearance mechanisms; Short retention time Blurred vision
Intravitreal	Direct injection into the vitreous humour	Localized drug delivery and maintained at a high therapeutic concentration Minimal off-target	Painful process because the injections Frequent injections lead to severe complications
Periocular	Primarily via the trans-scleral pathway	Less painful Bypassing the corneal barrier to achieving adequate therapeutic drug levels The integrity of the eyeball is not affected	Tissue hemorrhage Systemic side effects Rapid clearance
Suprachoroidal	Hollow microneedle injection targeting the choroidal layer	Drug effects at sites maximized by sclera bypassing	High requirements for operation Side effects because of the injections

Systemic	Reach of the choroid through the systemic circulation	Better patient compliance	Low bioavailability Drug-related toxicity because of administration of high doses

2. SLN (Solid Lipid Nano-Particle)

Lipids have been used as excipients or drug delivery carriers to accommodating lipophilic drugs and improve their poor physiological water solubility.[26] For hydrophilic drugs, water-in-oil emulsions and microemulsions have been extensively investigated to dissolve them for potential ophthalmic drug delivery. Although microemulsions have been known to scientists since 1928, their potential use in ocular dosing has only been explored in the last decade. Despite their simple preparation, easy sterilization and modest stability, the use of microemulsions in the administration of ophthalmic drugs is limited by the choice of well-tolerated ingredients. Oil-in-water emulsions and microemulsions require a high concentration of surfactant to ensure the stability of the formulation. This limits their suitability for ophthalmic administration, as surfactants are generally not well tolerated.[27] Müller and Lucks were the first to patent SLNs (1996). Since then, they have drawn the attention of several researchers as a stable, trustworthy, and non-toxic particle drug delivery system. In nanoscale locations, SLNs are arranged into a solid lipid core that enables drug stability with a surfactant layer. [28] SLN has several advantages over other colloidal carriers, such as the ability to control drug release, drug targeting, long-term stability, good drug loading (ie hydrophilic or lipophilic), lack of biotoxicity use of physiological lipids, possibility of sterilization with autoclave processing and easy large-scale production.[29] In addition, due to their nanosize range, SLNs can be an effective ocular drug delivery system, improving corneal absorption, improving ocular bioavailability, increasing ocular retention time, and providing a sustained drug release profile.[30]

2.1 Types of SLN's

Solid lipid carriers, also known as lipid nano-particles, are a type of drug delivery system used to encapsulate and deliver various active compounds, including pharmaceuticals, nutraceuticals, and cosmetics. They offer several advantages such as improved drug solubility, bioavailability, and controlled release. There are different types of solid lipid carriers, each with unique characteristics and applications. Here are some common types:

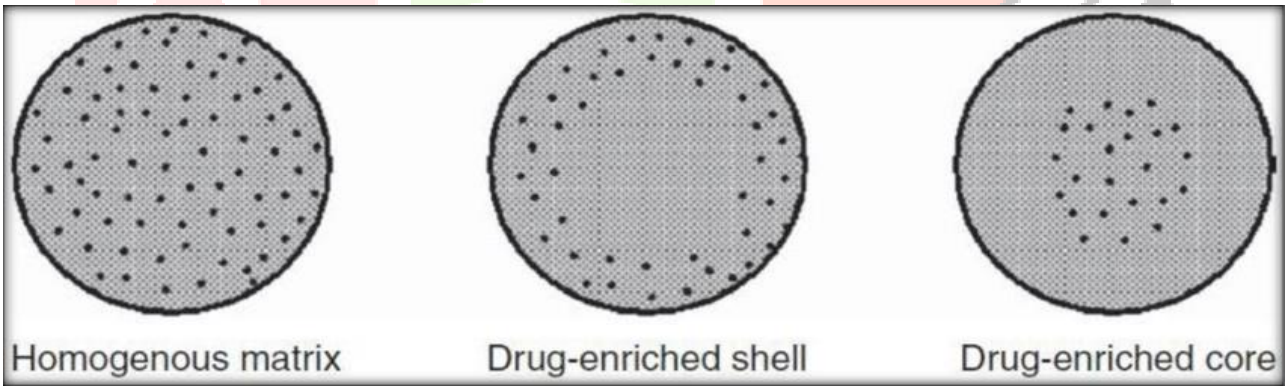

Fig No 2: Types of SLN: (I) Homogeneous Matrix Model (II) Drug-Enriched Model and (III) Drug-Enriched Core Model [31,32]

2.1.1 Homogenous Matrix Type SLN's

Solid solution model, also called homogeneous matrix model obtained when the drug is homogeneous dispersed in the lipid matrix as molecules or amorphous clusters This model is often described for lipids nano-particles produced by cold homogenization technology, or if highly lipophilic drugs are added so that a the heat homogenization technique can also be used without the use of surfactants or drug-dissolving molecules. When cold homogenization technology is used, solved the drug is dispersed in the basic lipid. When exposed to high pressure homogenization, mechanical mixing results formation of lipid nano-particles with a homogeneous matrix. A similar result is obtained when lipid droplets are generated hot homogenization technology is quickly cooled; drops tend to crystallize and there is no phase difference between them drug and lipid. Such models are suitable inclusion of extended-release drugs items.[32]

2.1.2 Drug-enriched shell Type SLN

A schematic of the drug-enriched shell model is illustrated. The drug-enriched shell is a lipid core surrounded by a drug-enriched outer shell. Such a structure is obtained when hot liquid droplets cool rapidly forming lipid nanoparticles such as as a result of phase separation. Medicinal peel morphology can be explained by lipid precipitation a mechanism that occurs during production and the redistribution of the drug that occurs during the cooling phase. After warm homogenization, each drop is a mixture of molten lipid and drug. Rapid cooling accelerates the precipitation of lipids in the core and at the same time increases the drug concentration in the outer liquid lipid. As a result of complete cooling, a drug-enriched shell precipitates. This structural model is appropriate inclusion of rapid-release medications. Such rapid release is highly desirable for dermatological SLN dosage forms that require greater drug penetration In addition to the occlusive effect of SLN. [31] Checked the release of clotrimazole from the topical SLN formulation was due to the drug-enriched shell structure .[33] Solvency drug in a mixture of surfactant and water raised temperature is another factor that can affect precipitation drugs in the shell. During hot homogenization the drug partially moves out of the lipid core due to this increase solubility in surfactant solution. However, the solubility of the drug in the surfactant solution decreases as the dispersion cools. This leads to drug enrichment in the shell in some cases where solidification of the lipid core has already begun.[32]

2.1.3 Drug-enriched core model of SLN

The drug-enriched core model is obtained when the recrystallization mechanism is the opposite of that described in the drug-enriched shell model. Schematic representation of a drug-enriched nuclear model. This morphology is obtained when the drug tends to crystallize before the lipid. The drug dissolves in the lipid melt close to its saturation solubility. Subsequent cooling of the lipid emulsion causes supersaturation of the drug in the lipid melt; this results in drug recrystallization before lipid recrystallization. Further cooling leads to lipid recrystallization, which forms a membrane around the already crystallized drug-enriched core. This structural model is suitable for drugs that require sustained release over a period of time according to Fick's law of diffusion.[34]

2.2 Morphology of SLN

2.2.1 Transmission electron microscopy (TEM)

TEM evaluates particle morphology by examining it electrons passing through the sample. The image is obtained by interpreting the interaction of electrons passing through the sample, which is visualized by an imaging device or detected by a special sensor. nano-particles can solubilize lipids in drug-enriched shell-dissolved SLN at room temperature. Phase separation solidification at 70 °C. An explanation of the burst release associated with SLNs in the release profile of solid lipid nano-particles for ophthalmic drug delivery can be visualized by TEM after cryofracture and freezing.[23,28]

2.2.2 Scanning electron microscopy (SEM)

This method provides excellent resolution and is simpler sample preparation procedure for morphological study of SLNs SEM measures electrons transmitted from the particle surface to evaluate their morphology [23,28]

2.2.3 Atomic force microscopy (AFM)

AFM creates a three-dimensional image of nano-particles. It is a very sensitive device and a spatial resolution of up to 0.01 nm can be achieved by measuring the force between the tip and the particle surface. [23,28]

2.3 Preparation of SLN

Various methods are used to prepare solid lipids nano-particles are listed below:[35-41]

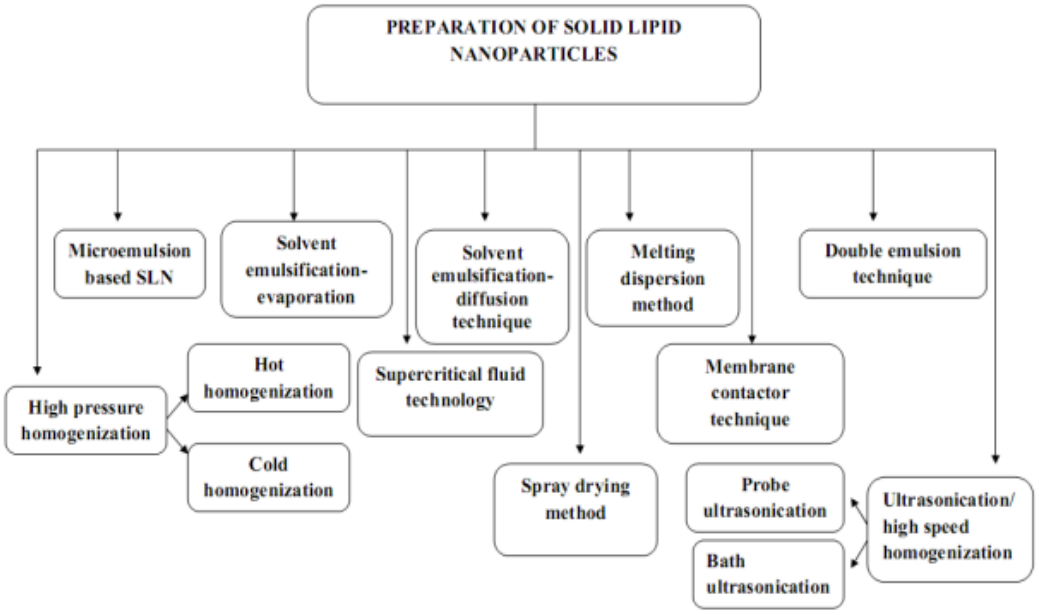

Fig no.3: Methods of preparation of solid lipid nano-particles [Error! Reference source not found.]

For SLN used for the ocular drug delivery following specific methods are use;

2.3.1 HIGH PRESSURE HOMOGENIZATION

HPH is a suitable method for SLN, NLC and LDC and can be made at an elevated temperature (hot HPH technology) or at room temperature (cold HPH technique). Cavitation that reduce particle size and turbulences In high pressure homogenization technology lipids are forced through high pressure (100-200 bar). a narrow gap of a few microns. So the shear stress and cavitation (due to sudden pressure drop) is forces that cause the particle to break into submicrons area Typically, the lipid content is between 5-10% At this concentration, it does not cause problems homogenizer High pressure homogenization is not visible any scaling problem. There are basically two approaches For the production of SLN by high-pressure homogenization, hot and cold homogenization techniques.

A) Hot Homogenization:

For the hot homogenization technique, the drug was loaded the molten lipid is dispersed by mixing with a high shear device (eg Ultra Turrax) in an aqueous surfactant solution identical temperature. The resulting pre-emulsion is homogenized with a homogenizer with a piston gap (e.g. Macron LAB 40 or Macron LAB 60 or APV-2000) and the prepared warm o/w Nano emulsion is cooled to room temperature temperature at room temperature, the lipid recrystallizes and leads to SLN formation.

B) Cold Homogenization:

Cold homogenization is performed with a solid drug containing lipids and is therefore called suspension milling. Cold homogenization was developed to avoid: temperature-induced drug degradation, distribution of hydrophilic drug from the lipid phase to the aqueous phase. Complexity of the Nano emulsion crystallization step leading to multiple modifications and/or supercooled melts. The first stage of preparation is the same as hot homogenization, which involves spreading or dissolving or drug dissolution in molten lipid. Then medicine the lipid mixture is rapidly cooled either by liquid nitrogen or dry ice.The solid lipid drug is ground in a mortar or ball mill to micron size (50-100 microns) and these micro particles are dispersed in a cooled emulsifying solution resulting in a pre-suspension. This pre-suspension is then homogenized in a high-pressure chamber or under a chamber the temperature at which the cavitation force is strong enough degrades micro particles into SLNs. This process avoids or minimizes lipid melting and thus minimizes loss of the hydrophilic drug to the aqueous phase. Another method minimize loss of hydrophilic drug to the aqueous phase replace water with other substances (eg oil or PEG 600). low solubility of drugs. Compared to warm homogenization, particle size

in cold homogenization and the polydispersity index (wider size distribution) is more. Cold homogenization only reduces heat exposure to the drug, but not completely melting the lipid/drug mixture in the first step preparation

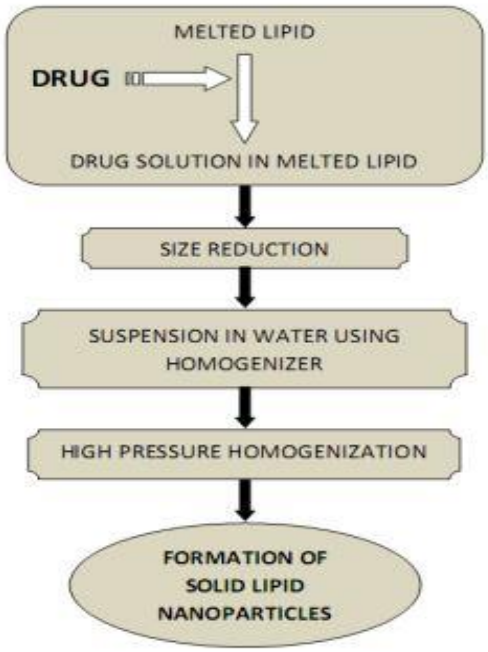

Fig No 4: Process of cold homogenization

Double Emulsion Technique (W/O/W Double Emulsion)

Double w/o/w emulsion is a relatively new method which has been used in manufacturing in recent years Nano emulsions and SLNs[43] There is no heating during the process, so it is suitable for hot substances. Good quality SLNs can be prepared by adjusting the sonication intensity. The only disadvantages of this method are the use of an organic solvent and the possibility of metallic impurities from the sonicator.[44]. The method involves dissolving the drug in an aqueous solution.[43] The aqueous solution is then emulsified into an oil phase containing lipids (lipids) dissolved in an organic solvent to form a primary w/o emulsion. The primary w/o emulsion is then dispersed in an aqueous solution containing a surfactant. The w/o/w double emulsion system is mechanically stirred to allow complete evaporation of the organic solvent until SLNs are formed.[23]

Solvent emulsification- evaporation

Using the solvent emulsification-evaporation method, the lipophilic material and the hydrophobic drug were dissolved in a water immiscible organic solvent (e.g., cyclohexane, dichloromethane, toluene, chloroform) and then there is emulsified at high speed into the aqueous phase homogenizer Increases efficiency perfectly during emulsification a crude emulsion was passed through micro fluidizer. After that, there were organic solvents vaporized with mechanical agitation at room temperature and under reduced pressure (eg, in a rotary evaporator), leaving the lipid Precipitation of SLNs. Here, the average particle size depends of the lipid content of the organic phase. A very small particle size can be obtained with low lipid loading (5%) relative to the organic solvent. The great advantage of this technique is the avoidance of thermal stress, which makes it very suitable heat-labible drugs. The clear disadvantage is the use an organic solvent that can interact with drug molecules and limited the solubility of the lipid in an organic solvent. [42]

Solvent emulsification-diffusion technique

This method is based on the miscibility with water certain organic solvents such as butyl lactate or benzyl alcohol as the oil phase [45,46] A primary oil-in-water emulsion containing the drug and a solution of the lipid phase in a water-miscible solvent is prepared. This emulsion is then transferred water the hypothesis is that if the drivers an into the aqueous phase, the water-miscible solvent diffuses. Thus, the lipophilic material dissolved in the solvent Solidifies due to solvent diffusion from the droplets to the continuous phase. This method used to encapsulate insulin in glyceride monostearate solid lipid micro- and nano-particles using isobutyric acid as a

water-miscible solvent. The capture efficiency was remarkably satisfactory (80%), but the burst effect, which released 20% of the drug, suggested the presence of insulin on the surface of the particles rather than inside. The method is reliable for the entrapment of lipophilic and hydrophilic drugs when optimized. [46]

3. BARRIERS FOR OCUAR DELIVERY:

3.1 Drug loss from the ocular surface

Tear fluid flows after instillation removes absorbed compounds from the surface of the eye. Even although the tear flow rate is only about 1 µl/min, the extra fluid that is dripped will flow nasolacrimal ducting quickly in minutes. Secondly the source of unproductive drug withdrawal is its systemic absorption instead of absorption through the eye. Systemic absorption can occur either directly from the conjunctival sac through local blood capillaries or after the solution flows into the nose pit.[47]

3.2 Lacrimal fluid-eye barriers

The corneal epithelium limits drug absorption tear fluid in the eye. Corneal epithelial cells form tight junctions that limit the penetration of para cellular drugs. Therefore, lipophilic drugs usually have at least an order of magnitude greater corneal permeability than hydrophilic drugs. In general, the conjunctival epithelium is more leaky than the cornea, and its surface area is also nearly 20 times that of the cornea.[47]

3.3 Blood-ocular barrier

The eye is protected against xenobiotics into the bloodstream through the blood-eye barriers. These obstacles are two parts: the blood-aqueous barrier and the blood-retinal barrier. The anterior blood-ocular barrier consists of endothelial cells in the uveum (The middle layer of the eye under the sclera. Consists of the iris, iris and choroid). This barrier prevents plasma albumin from entering the ventricular fluid and also limits the movement of hydrophilic drugs from the plasma to the aqueous humor. The posterior barrier between the blood flow and the eye consists of the retinal pigment epithelium (RPE) and the dense walls of the retinal capillaries. Unlike retinal capillaries, choroidal vessels have extensive blood flow and leaky walls. Drugs easily enter the extravascular space of the choroid, but limit it after retinal distribution RPE and retinal endothelium.[47]

4. MECHANISM OF OCULAR DRUG ABSORPTION

Medicines administered by instillation must penetrate eye and mainly through the cornea extra corneal pathways. These noncorneal pathways include drug diffusion through the conjunctiva and sclera and appears be especially important for medications that do not work well absorbed through the cornea.[48]

4.1 Corneal permeation

Penetration of drugs through the cornea the film comes from a pre corneal space.Various barrier to drug absorption Tears have a direct effect on the effectiveness of the drug absorption into the eye. Productive absorption most ophthalmic drugs are the result of a diffusion process through the cornea. Absorption efficiency the process depends on speed and scope ocular transport processes. Flow of any drug molecule through the biological membrane depends on the physico-chemical properties of the penetrating molecule and its interaction with the membrane. To what extent the transport or absorption process must also be done physiological mechanism of pre corneal fluid drainage or Sale Regarding drug penetration through the cornea, the cornea can be considered to consist of three primary layers (epithelium, stroma, and endothelium). The epithelium and endothelium contain about 100 times more lipid material than the stroma. Thus, the resistance offered by individual layers varies greatly depending on the physicochemical properties of the diffusing drug. The lipoid epithelium represents a diffusion barrier that offers high resistance to ionic or other water-soluble or polar species. In comparison, compounds of relatively low polarity are exposed to higher diffusion resistance in the hydrophilic stromal layer. This oft-cited concept of drug permeability across the corneal membrane is called the "differential solution concept."[47]

4.2 Non-corneal permeation

The main mechanism of drug penetration is dura membrane diffusion, probably through the intercellular space aqueous medium in the case of a structurally similar cornea stroma Therefore, there is a possibility of a distribution mechanism cannot be deleted. Although like the cornea, the conjunctiva consists of an epithelial layer

that covers the one below in the stroma, the conjunctival epithelium offers significantly less resistance than the corneal epithelium.[47]

5. Case studies

5.1 Voriconazole ocular delivery based on SLN

The study found that lipophilic drugs like voriconazole can be incorporated into solid lipids using Tween 80 as a stabilizer. The research explored the use of voriconazole-loaded solid lipid nano-particles in the ultrasonic method and microemulsion techniques. Carbopol 934 was used as a controlled release agent, resulting in SLNs below 400 nm with good PDI and negative zeta potential. The nano-particles produced a biphasic release pattern, with an optimized formulation providing a shelf life of over 2 years. [49]

5.2 Tobramycin ocular delivery based on SLN

It was hypothesized that SLNs could improve the bioavailability of TOB in the eye based on previous evidence that SLNs could improve duodenal absorption of TOB. [50,51] A topical SLN-based ophthalmic containing an ion-pair complex of TOB with hexadecyl phosphate was developed using a hot o/w macro emulsion technique, purified by dialutrafiltration, and freeze-dried to determine drug loading efficiency. The re-dispersed SLNs were sterilized with saturated steam for 15 min at 121 °C. Intraventricular TOB concentration was determined after local administration. An HPLC method was developed for the quantitative measurement of TOB. Fluorescence labeling was used to determine SLN residence time in male New Zealand albino rabbits. Ocular tolerance and the degree of irritation of TOB-containing SLNs were investigated in male New Zealand white rabbits using a previously developed method based on a blink score scale.[52] and SLN spread were tolerated without any irritation. The average particle size of the TOB-loaded SLNs was measured and found to be ~80 nm with a polydispersity index of only 0.12. Periocular retention studies showed the presence of fluorescent SLNs in the rabbit eye for more than 1 h compared to a fluorescent solution. that was quickly washed into the eye from the surface.

Ocular bioavailability of SLN-conjugated TOB was significantly higher than that of eye drops. TOB loaded SLNs had a Cmax of 36.30±1.09, a Tmax of 4 hours and AUC 155.08±4.31. Cmax increased 1.5 times, Tmax 8 times and AUC 4 times. Increased ocular bioavailability may be due to increased ocular occupancy time and trapping of SLNs in the mucin coat epithelium due to their smaller particle size leading to sustained release of TOB and potentially increased surfactant penetration into the eye, in this case epicuron 200, soya phosphatidyl choline [50]

6. Application of SLN

Solid lipid nano-particles (SLNs) are nano-particles composed of solid lipids that have gained significant attention in various fields due to their versatile applications. Some key applications of SLNs include:

6.1 Other Application:

1. Drug Delivery:

SLNs are used as carriers in drug delivery systems. They improve the bioavailability of poorly water-soluble drugs and provide a controlled release that improves therapeutic efficacy. [53]

2. Cosmetics and Skincare:

Because SLNs can encapsulate active substances and ensure improved skin penetration and prolonged release, they are used in cosmetic and skincare products. [54]

3. Food Industry:

To improve the stability and targeted distribution of bioactive substances, vitamins, and flavorings within the body, the food industry uses SLNs to encapsulate them. [55]

4. Agrochemicals:

In order to enable controlled release and lessen environmental damage, SLNs are being investigated as pesticide and agrochemical carriers. [56]

5. Imaging and Diagnostics:
For use in theranostics, medical imaging, and diagnostics, SLNs can be loaded with contrast agents or imaging dyes. [57]

6. Gene Therapy:
SLNs have the potential to be used in gene delivery systems, which would enable the effective transfer of genetic material to target cells. [58]

7. Vaccine Delivery:
By acting as vaccine carriers, SLNs can improve the immunogenicity and stability of antigens. [59]

8. Cancer Therapy:
Research is being done on the use of SLNs for targeted medication delivery in cancer therapy, which will allow anticancer medicines to be delivered selectively to tumor areas. [60]

9. Nutraceuticals:
By encasing them in SLNs, nutritional supplements and functional meals can better absorb and contain nutraceuticals. [61]

10. Personal Care Products:
To improve the delivery of active substances, SLNs are added to personal care products like sunscreens, lotions, and shampoos. [62]

6.2 OCULAR APPLICATION
SLNs have received considerable attention in the field of ophthalmic drug delivery because there ability to improve in drug sustained release, bioavailability, and solubility. Here are some applications of solid lipid nano-particles in ocular drug delivery systems

1. Improved drug solubility:
SLNs can encapsulate both hydrophobic and hydrophilic drugs, improving their solubility and stability, which is particularly useful for drugs with poor water solubility.

2. Prolonged drug release:
SLNs can be designed to provide sustained drug release, reducing the need for repeated administration, which can be an important advantage for ocular drug delivery.

3. Enhanced drug penetration:
SLNs can improve drug penetration across the cornea, which is a major challenge in ocular drug delivery. Their small particle size and lipid composition can enhance drug bioavailability in the anterior and posterior segments of the eye.

4. Reduced irritation and toxicity:
SLNs are considered biocompatible and non-toxic, making them suitable for ocular applications and reducing the risk of irritation and adverse effects.

5. Targeted drug delivery:
SLNs can be modified with ligands or surface coatings to facilitate targeted drug delivery to specific ocular tissues, such as the retina or the anterior segment.

6. Preservation of drug stability:
SLNs can protect drugs from degradation by encapsulating them in a lipid matrix, enhancing drug stability during storage and administration.

7. Minimized systemic absorption:

SLNs can help reduce the systemic absorption of drugs, minimizing potential systemic side effects and enhancing the therapeutic effect at the target site.

8. Treatment of various ocular diseases:

SLNs have been investigated for the delivery of drugs to treat conditions like glaucoma, age-related macular degeneration, diabetic retinopathy, and ocular infections.

9. Combination therapy:

SLNs allow for the co-encapsulation of multiple drugs, enabling combination therapy for complex ocular diseases. [63-66]

7. FUTURE PROSPECT & CONCLUSION

As we delve into the promising realm of solid lipid nano-particles (SLNs) for ocular drug delivery, the future holds immense potential for advancements and innovations in this field. Several avenues for further research and development emerge, paving the way for enhanced therapeutic outcomes and patient-centric solutions.

In conclusion, the exploration of solid lipid nano-particles for ocular drug delivery presents a fascinating journey into the convergence of nanotechnology and ophthalmic medicine. The remarkable progress made in understanding the potential of SLNs underscores their versatility and applicability in addressing the challenges associated with traditional drug delivery to the eye.The reviewed literature reveals that SLNs offer numerous advantages, including improved bioavailability, sustained release, and reduced systemic side effects. However, challenges such as stability, scalability, and long-term safety profiles must be addressed to ensure the successful translation of SLN-based formulations from the laboratory to clinical settings. As we look to the future, the field of ocular drug delivery stands on the cusp of transformative developments. The integration of advanced technologies, tailored formulations, and a deeper understanding of ocular physiology will undoubtedly propel SLNs into the forefront of therapeutic strategies for ocular diseases.

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